Foreign Bodies in Small Arteries after Use of an Infusion Microcatheter

Stanley L. Barnwell, Anthony N. D'Agostino, Steven L. Shapiro, Gary M. Nesbit, and Jordi X. Kellogg

Summary: Over a 31-month period, we performed four neurointerventional procedures after which unexpected foreign bodies were noted in multiple arteries. All four procedures had in common the use of Fastracker-18 infusion microcatheters. Histologically, the intravascular debris looked strikingly similar to the hydrophilic coating on the catheter. An in vitro test mimicking clinical use of the microcatheter revealed that the hydrophilic coating can separate from the catheter. Until the coating is refined to make it more resistant to stripping, it may be advisable to reduce the amount of back-and-forth movement of these microcatheters if they have been positioned through guide catheters with small inner diameters and angled tips.

Index terms: Catheters and catheterization, complications; Foreign bodies; Iatrogenic disease or disorder

Between October 1994 and October 1996, four autopsy cases revealed unexpected foreign bodies in small arteries after neurointerventional procedures using the Fastracker-18 infusion microcatheter (Target Therapeutics, Fremont, Calif). These cases included three procedures involving local intraarterial thrombolysis for acute thromboembolic stroke and one preoperative embolization of a tentorial meningioma. All the procedures required multiple manipulations of the microcatheter in tortuous anatomy through a 7F Positrol II Berenstein catheter (Bard, Billerica, Mass), a 5.5F Norman catheter (Cook, Bloomington, Ind), a 6F Multipurpose Envoy guiding catheter (Cordis, Miami, Fla), or a 5F Imager Berenstein catheter (Boston Scientific, Watertown, Mass). The intravascular debris bore a striking similarity to the material composing the hydrophilic coating on the Fastracker-18 infusion microcatheter. In vitro manipulation of the Fastracker-18 infusion microcatheter in the 7F Positrol II Berenstein catheter lightly wedged against the wall of a test tube filled with water caused the hydrophilic coating to separate from the microcatheter.

Representative Cases

Case 1

A 53-year-old woman with a history of atrial fibrillation presented with sudden onset of a left hemiplegia. The computed tomographic (CT) scan was normal. An angiogram showed thromboembolic occlusion of the right internal carotid artery at the bifurcation. A Fastracker-18 infusion microcatheter was navigated over a Taper 14 Flex tip guidewire (Target Therapeutics) through a 5.5F Norman catheter (Cook) into the occluded vessel. The insides of both the guide catheter and microcatheter were continuously flushed with a heparinized saline solution using two rotating hemostatic valves connected to pressure bags. Local intraarterial thrombolysis was performed about 5 hours after symptom onset. The microcatheter was maneuvered several times through the thrombus while 200 000 U urokinase was infused in a pulse-spray fashion as described previously (1).

After about 2 hours, thrombolysis with recanalization was obtained. Five hours later, the patient became comatose. A CT scan showed a large hemorrhage in the basal ganglia. Despite surgical evacuation of the hematoma the patient made no improvement and died 72 hours later. A complete autopsy, including brain examination, was performed. Sections of the right hemisphere stained with hematoxylin-eosin showed basophilic, nonrefractile, filamentous material in many small arteries. The approximately 2-μm-thick filaments were twisted and folded in the vascular lumens. Some foci had an associated giant cell foreign body inflammatory response, and this material occluded the blood vessel.

Case 2

A 58-year-old man became comatose 3 hours after onset of dizziness and a hemiparesis. A hyperdense basilar

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From the Division of Neurosurgery and the Dotter Interventional Institute (S.L.B., G.M.N., J.X.K.) and the Department of Pathology (A.N.D., S.L.S.), Oregon Health Sciences University, Portland.

Address reprint requests to Stanley L. Barnwell, MD, PhD, Division of Neurosurgery, Mail Code L-472, Oregon Health Sciences University, 3181 SW Sam Jackson Park Rd, Portland, OR 97201.

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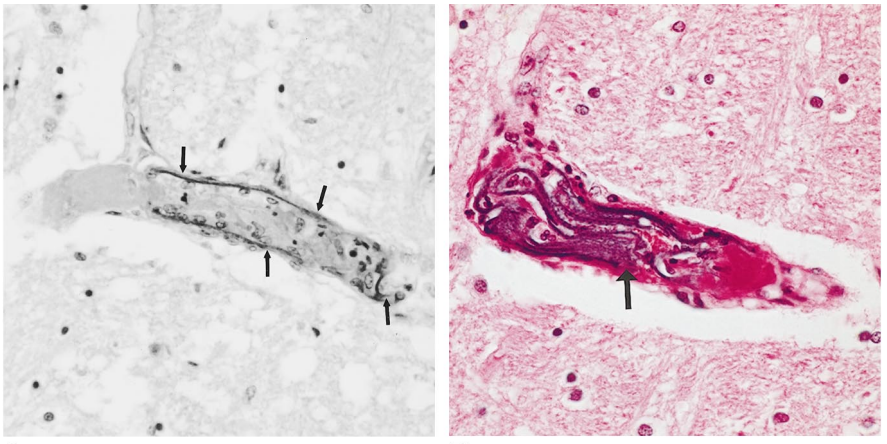

Fig 1. *A*, Photomicrograph of the brain from case 2 shows intravascular foreign bodies (*arrows*) filling the blood vessel (hematoxylin-eosin, original magnification ×500).

B, Photomicrograph of the brain shows another artery filled with similar debris (hematoxylin-eosin, original magnification ×500). Note the granular appearance of the foreign body where it lies flat across the section (*arrow*).

artery noted on the CT scan was found to have a distal thromboembolic occlusion at angiography. A Fastracker-18 infusion microcatheter was navigated over a Dasher-14 steerable guidewire (Target Therapeutics) through a 7F Positrol II Berenstein catheter into the clot. Local intraarterial thrombolytic therapy was begun about 10 hours after the coma began. Urokinase, 1.25 million U, was infused into the clot with multiple passes of the microcatheter through the clot. No significant change in the appearance of the angiogram was noted, and the procedure was stopped. The patient made no neurologic improvement and died about 48 hours later. An autopsy was performed and the brain examined. Residual thromboembolus was found in the basilar artery. Pontine sections contained numerous foci of intravascular foreign material, which had an appearance identical to that of the filaments described in case 1. Fibrin thrombi, occluding the vessels, were also noted to be associated with the foreign substance (Fig 1).

Case 3

A 53-year-old woman presented with ataxia. Contrast-enhanced magnetic resonance (MR) imaging showed a tentorial tumor with a nonenhancing core. At angiography, the tumor was found to receive its blood supply from a branch of the occipital artery and the posterior division of the middle meningeal artery. Both these vessels were catheterized with the Fastracker-18 infusion microcatheter and a Dasher-14 steerable guidewire, introduced through a 5F Imager Berenstein catheter, and embolization was performed with polyvinyl alcohol particles and platinum coils. The next day, resection of the tumor was performed. An intraoperative frozen section confirmed the diagnosis of meningioma. Also identified in the biopsy specimen were the same intravascular basophilic filaments described in the previous cases.

Case 4

A 66-year-old man experienced several weeks of dizziness before a right-sided hemiplegia and lethargy developed in May. A CT scan showed calcified vessels, and an angiogram revealed thromboembolic occlusion of the distal left vertebral and basilar arteries. A 6F Multipurpose C Envoy guidecatheter (Cordis) was placed in the left vertebral artery. A Fastracker-18 infusion microcatheter was navigated over a Dasher-14 steerable guidewire into the occluded artery, and over 30 minutes a combination of 500 000 U of urokinase and mechanical disruption resulted in recanalization of the basilar artery. A stenosis of the distal vertebral artery was treated by angioplasty with a 3-mm-diameter, 15-mm-long Fastealth balloon dilatation catheter (Target Therapeutics). The patient made minimal improvement for 3 days, then deteriorated. An MR image showed bilateral thalamic and pontine infarcts. He died after 13 days. Autopsy sections showed multiple intravascular foreign bodies with evolving infarcts in the pons and thalamus. These foreign bodies are identical to the ones in the previous cases.

Discussion

Materials common to the first two cases were urokinase (Abbokinase, Abbott Laboratories, North Chicago, Ill), Isovue-300 (Bracco Diagnostics, Princeton, NJ), and the Fastracker-18 infusion microcatheter. In the labeling of the commercial preparation of urokinase, reference is made to a filamentous material that may be present (2); however, no postmarketing reports have mentioned any adverse events related to this material, and the substance has never been identified to the manufacturer (personal communication, Helen Eliopoulos, Abbott Laboratories, October 1996). Because urokinase was not used in the third case, the only common sources of the foreign body appeared to be the contrast agent or the Fastracker-18 infusion microcatheter. Commercial preparation of the contrast agent involves terminal filtering through a 0.2-μm filter, which should eliminate

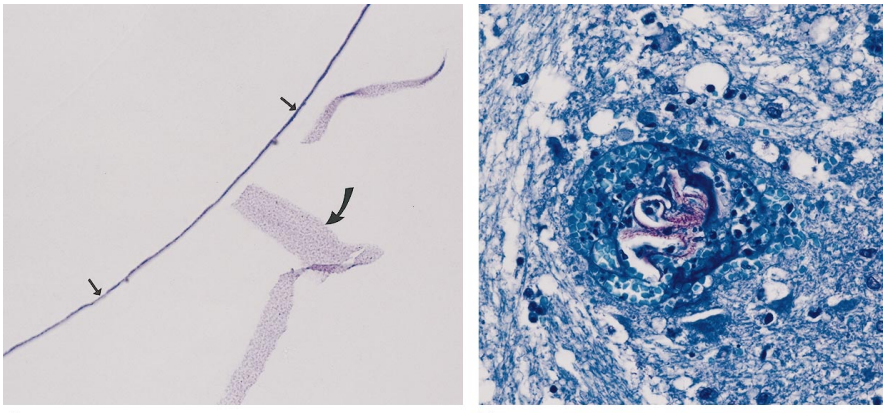

Fig 2. *A*, Photomicrograph of the Fastracker-18 microcatheter shows staining of the coating (*straight arrows*) (toluidine blue, original magnification ×500). A strip of the coating has separated from the catheter and has a granular appearance (*curved arrow*).

B, Photomicrograph of the brain from case 2 shows intravascular foreign body with similar staining appearance as the catheter (toluidine blue, original magnification ×500).

foreign material of the size seen in our cases. In addition, any precipitation of the contrast material would produce an optically active crystal different from the material of interest (personal communication, Bruce Davidson, Bracco Diagnostics, January 1997). More definitive testing of the material on the pathologic slides (ie, by Fourier transform infrared spectroscopy) probably was not possible because of the small size and small volume of the material (personal communication, Greg Strossman, Charles Evans and Associates, Redwood City, Calif, January 1997).

Left with no explanation for the foreign bodies found in the arteries, we studied the Fastracker-18 infusion microcatheter. This microcatheter was hydrated in the fashion recommended by the manufacturer. A distal section of the catheter was then sectioned in short lengths, processed automatically with routine histologic specimens, embedded in paraffin, cut in 2-μm-thick sections, and stained with hematoxylin-eosin. At microscopy, the catheter coating was found to stain in a granular basophilic fashion, which was remarkably similar to the intravascular material found in the four cases. Even the approximately 2-μm thickness of the coating compared well with that observed in the tissue sections. A separate stain of the catheter and the material from case 2 using toluidine blue also produced a virtually identical match between the catheter coating and the intravascular debris (Fig 2).

To study whether the Fastracker-18 infusion microcatheter could have been the source of this material, we performed a test designed to mimic the clinical use of this catheter. The distal 10-cm end of the microcatheter was cut and placed through the distal end of a 7F Positrol II Berenstein catheter. The combination was then placed in a glass tube filled with water, and with the end of the Berenstein catheter wedged lightly against the wall of the glass tube, the microcatheter was pulled back and forth through the end of the catheter. The tip of the Berenstein catheter was wedged against the glass tube to the degree that mimics its use in vivo. We encountered some resistance to pulling and pushing, but not an untoward amount and not to a degree that would stretch the microcatheter. The microcatheter was then prepared as previously described for microscopic examination. Sections that had been pulled and pushed through the end of the Berenstein catheter showed large areas in which the hydrophilic coating was missing (Fig 3A). Other sections showed peeling of the hydrophilic coating (Fig 3B). These fragments again bore a striking similarity to the intravascular foreign bodies in the three cases. Microscopic findings from control catheters not subjected to this test showed intact coating.

All four of our cases required significant movement of the microcatheter through an angled tip guidecatheter in tortuous anatomy. In these arteries, the microcatheter probably was wedged between the wall of the artery and the tip of the guidecatheter. Movement of the microcatheter may have caused the hydrophilic coating to strip off the catheter and into the blood vessel. There were no known adverse clinical effects of this foreign intravascular material, although the size and number of the blood vessels blocked is of concern. In case 2, the pons showed infarction in the region of the foreign bodies, although the cause of death was probably related to the distal basilar artery thromboembolus.

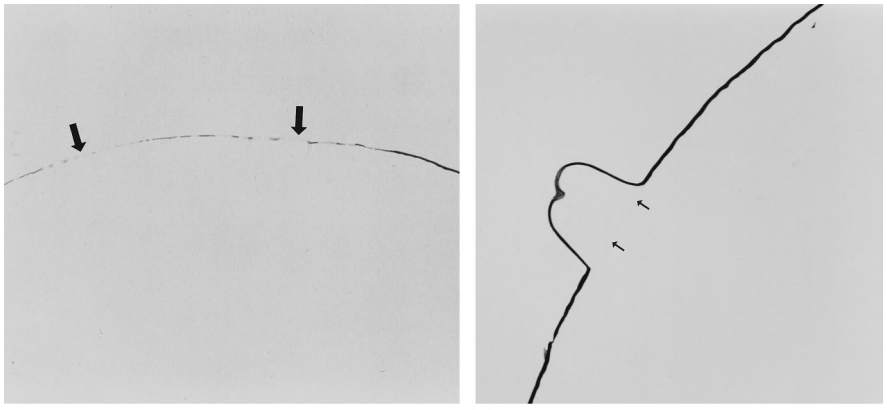

Fig 3. *A*, Photomicrograph of the Fastracker-18 microcatheter shows the hydrophilic coating has been removed during the test, leaving large areas of the catheter denuded (*arrows*) (hematoxylin-eosin, original magnification ×500).

B, Photomicrograph of the Fastracker-18 microcatheter in which another section shows peeling of the hydrophilic coating from the body of the catheter (hematoxylin-eosin, original magnification ×500). The outline of the catheter from which the hydrophilic coating has separated is barely visible (*arrows*).

In case 4, evolving infarctions were seen in the pons, and a hemorrhagic infarction was present in the thalamus, where the foreign bodies were found. The hydrophilic coating adds significantly to the maneuverability of microcatheters through tortuous cerebral blood vessels, and the separation of the coating may in part explain the apparent loss of function of these catheters when they are used for extended periods in tortuous anatomy. By the same token, microcatheters without the hydrophilic coating are often not capable of navigating through such tortuous anatomy.

Further testing needs to be performed to see if this problem occurs with other microcatheters with hydrophilic coatings and whether the coating can be reformulated to prevent it from stripping off the catheter. It is not known whether guidecatheters with straighter tips would also cause this separation to occur. The guidecatheters with straighter tips may be less likely to cause separation because of decreased friction between the tip and the wall of the blood vessel. The procedure we described is a simple and inexpensive way to test this coating in a manner that mimics use of the microcatheter in vivo. The manufacturer is actively evaluating the coating and ways in which it can be made more adherent to the catheter (personal communication, Robert Hergenrother, Target Therapeutics, May 1997). Until additional testing can be done, it would be advisable to limit the amount of back-and-forth movement of this microcatheter through tortuous anatomy when used with guide catheters with angled tips.

References

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